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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,234	04/06/2001	Tae-Shin Park	0136/OJ067	3081

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EXAMINER	
TUNG, JOYCE	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 12/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,234	PARK ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-25,27-29 and 31-38* is/are pending in the application.

4a) Of the above claim(s) *12-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,27-29 and 31-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/30/2005 has been entered.

The applicant's response filed 9/30/2005 to the Office action has been entered. Claims 12-25, 27-29 and 31-38 are pending. Claims 25, 27-29, 31-38 are currently under examination.

2. Regarding the restriction requirement, based upon the reconsideration of the argument, the election of SEQ ID NO: 1 and 22-23 is withdrawn. As set forth in MPEP, Applications claiming only a combination of nucleotide sequences, such as set forth in example (B), will generally not be subject to a restriction requirement. The presence of one novel and nonobvious sequence within the combination will render the entire combination allowable. The combination will be searched until one nucleotide sequence is found to be allowable. The order of searching will be chosen by the examiner to maximize the identification of an allowable sequence. If no individual nucleotide sequence is found to be allowable, the examiner will consider whether the combination of sequences taken as a whole renders the claim allowable (See MPEP, 803.04[R-3]. Therefore, it is suggested to amend the language to indicate that it is a combination of SEQ ID NO: 1-19 used to make an array for the method of diagnosis of Human Papillomavirus infection.

3. Applicant's arguments with respect to the rejection of claims 25, 27-29, and 31-38 have been considered but are moot in view of the new ground(s) of rejection as set forth below.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 28, and 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 28 is vague and indefinite because it is unclear what is the definition of the phrase "position marker".

b. Claims 32-35 are vague and indefinite because it is unclear what is the antecedent basis of the phrase "a solid support" and whether or not the phrase "a solid support" is referred to the glass slide of claim 25. Clarification is required.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C 1029e),(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 25, 27, 29, 32-34 and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer et al (WO 95/22626, issued August 24, 1995), in view of Day et al. (Biochem. J., 1990, Vol. 267, pg. 119-123) and Lukhtanov et al. (6,339,147, issued October 15, 2002)

Meijer et al. disclose SEQ ID NO: 31 (which is identical to the instant SEQ ID NO:1) is a probe specific for detecting HPV-type 16 (See page 15 and 31). Meijer et al. indicate that this probe can be used in the rapid detection of high-risk HPV types and enhances detection by not allowing cross-hybridization (See pg 5 lines 20-23). Meijer et al. also disclose SEQ ID NO: 1 (See pg. 5, line 26) which is identical to instant SEQ ID NO: 22 and SEQ ID NO: 2 (See pg. 10, line 3) which is identical to instant SEQ ID NO: 23. These sequences are used as primer GP5 (See pg. 6, line 4-5) and primer GP6 (See pg. 10, lines 22-23).

Meijer et al. do not disclose that the primer is biotin labeled and using biotin-16-dUTP in detecting HPV.

Day et al. disclose the method of incorporation of biotin into the polymerase chain reaction products for the detection of the amplified DNA (See pg. 1990, column 1, second paragraph). The method applies the 5' biotinylated primer or biotin 16-dUTP to label the amplified products (See pg. 1990, column 1, second paragraph). The method also used second label, which is streptavidin-horseradish peroxidase (See pg. 1990, column 1, second paragraph)

Meijer et al. do not disclose that a DNA chip comprising probes having an HPV nucleic aid sequence attached to a glass slide.

Lukhtanov et al. disclose that the derivatized oligonucleotides are coupled to a solid support (See the Abstract). The invention is used for the capture and detection of nucleic acids using oligonucleotide attached to glass surfaces in array format (See column 7, lines 41-47). The oligonuleotide contains a nucleophilic amino group while the solid support contains aldehyde to form an Schiff base-type covalent linkage that attached the oligonucleotide to the solid support alternatively (See column 8, lines 27-37 and column 14, lines 15-19). Lukhtanov et al. also discuss the density of the oligonucleotides on the array (See column 14, lines 29-30) and derivatization of glass slides and preparation of oligonucleotide arrays on the glass slides (See column 23, lines 15-54).

None of the references above explicitly discloses that the concentration of the probe is between 100 and 300 pmol/ul on the aldehyde-derivatized surface of a solid support, the Schiff's base reaction between the amine and aldehyde groups is under an environment of between 30^0C and 40^0C and between 70% and 100% humidity.

However, Lukhtanov et al do disclose the ability to attach a high percentage of the oligonucleotide, for example, 60%, preferably about 90% to the semicarbazide moiety containing solid support and high coupling density on the unit of the solid support, for example, 10^4 oligonucleotide/um^2 and preferably 10^5 oligonucleotides/um^2 (See column 4, lines 25-37).

In addition, the method of Lukhtanov et al. involves the reaction of an Schiff base-type covalent linking reaction. Based upon the teachings of Lukhtanov et al., the limitations of the

claims regarding the temperatures and the humidity required for the reaction are inherent (See column 23, lines 30-36).

One of ordinary skill in the art would have been motivated to modify the method of Meijer et al. by using biotinylated primer and biotin-16-dUTP for detecting HPV as taught by Day et al. because the method of Day et al. dose not lose the amplification efficiency (See pg. 119, the Abstract) and by using the second label, streptavidin-horseradish peroxidase in sandwich assay (See pg. 1990, column 1, second paragraph), the assay does not need ~~for~~ separate labeled probe currently required in conventional sandwich assays. It would have been prima facie obvious to apply the biotinylated primer and biotin-16-dUTP in PCR reaction for the diagnosis of HPV on the DNA chip.

One of ordinary skill in the art would have also been motivated to modify the method of Meijer et al. by using a glass slide which has nucleic acid probe attached for the diagnosis of HPV infection as taught by Lukhtanov et al. because the array of Lukhtanov is via a Schiff base type bond formed between an NH_2 group attached either to the solid support or the oligonucleotide and an aromatic aldehyde attached to the other of the solid support and the oligonucleotide (See the Abstract) in which the Schiff base with aromatic-aldehyde bonds is stable, high percentage of oligonucleotide is contained on the solid support, specific attachment at either the 5'- or 3'- end is achieved and high coupling densities are obtained on unit surface (See column 4, lines 25-37). It would have been prima facie obvious to make the DNA chip with the probe attached to the glass slide for the diagnosis of HPV.

8. Claims 31 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer et al (WO 95/22626, issued August 24, 1995) in view of Day et al. (Biochem. J., 1990, Vol. 267,

pg. 119-123) and Lukhtanov et al. (6,339,147, issued October 15, 2002) as applied to claims 25, 27, 29, 32-34 and 36-37 above, and further in view of Sena et al. (US 5,273,881, issued December 28, 1993).

The teachings of Meijer et al., Day et al., Lukhtanov et al. are set forth in section 7 above. None of the references discloses the use of streptavidin-R-phycoerythrin.

Sena et al. disclose a diagnostic method for detecting a linear duplex DNA analyte (See column 3, lines 41-42). The method uses streptavidin with flurorescein label, R-phycoerythrin (see column 4, lines 39-46).

One of ordinary skill in the art would have been motivated to apply the streptavidin with fluorescein label, R-phycoerythrin as label in the method of Meijer et al. or the method of Day et al. as taught by Sena et al. because the streptavidin with flurorescein label, R-phycoerythrin was well known in the art to achieve the benefit of providing an effective biotin detection reaction. It would have been prima facie obvious to apply streptavidin-R-phycoerythrin for the diagnosis of HPV.

9. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer et al (WO 95/22626, issued August 24, 1995) in view of Day et al. (Biochem. J., 1990, Vol. 267, pg. 119-123) and Lukhtanov et al. (6,339,147, issued October 15, 2002) as applied to claims 25, 27, 29, 32-34 and 36-37 above, and further in view of Shalon et al. (US 2003/01112695, issued January 16, 2003).

The teachings of Meijer et al., Day et al., Lukhtanov et al. are set forth in section 7 above. None of the references discloses the use of a reducing agent, $NaBH_4$ to reduce excessive aldehyde which is not reacted with amine in the reaction

Shalon et al. disclose a method of determining the relative amounts of individual polynucleotide in a complex mixture of different-sequence polynucleotides. The polynuleotides after fluorescent labeling, are contacted under hybridization condition with an array of different DNA sequences disposed at discrete locations on a non-porous surface, at an array density of at least about 100 sequences/cm^2 (See the Abstract). The target is attached to a glass slide (See pg. 9, [0140]) in which $NaBH_4$ is used in the reaction (See pg. 9, ([0141]).

One of ordinary skill in the art would have been motivated to apply $NaBH_4$ in the oligonucleotide and the solid support coupling reaction of Lukhtanov et al. as taught by Sena et al. to make the DNA chip with the probes attached to the glass slides because the array of Shalon et al. has density of at least about 100 sequences/cm^2 where the different DNA sequences in the array are effective to hybridize to individual polynucleotides in the mixture (See the Abstract). It would have been prima facies obvious to use $NaBH_4$ in the reaction to make the DNA chip with the probes attached to the glass slide for the diagnosis of HPV.

10. The references of Roger et al. (Analytical Biochemistry, 1999, Vol. 266, pg. 23-30) and Joo et al. (Analytical Biochemistry, 1997, Vol. 247, pg. 96-101) are made of record as references of interests because these references teach the immobilization of oligonucleotide onto a glass support.

Summary

11. No claims are allowable.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
12/1/05

Joyce Tung
December 1, 2005